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Applicants : Howard J. Worman and Naoto Mamiya NOV 19 1999
Serial No. : 09/407,432 TECH CENTER 1600/2900
Filed : September 29, 1999 Group Art Unit:1646
For HCV CORE PROTEIN BINDING AGENTS FOR
TREATMENT OF HEPATITIS C VIRUS INFECTION



1185 Aveune of the Americas
New York, New York 10036
November 15, 1999

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (Exhibit 1). Copies of the disclosures listed below as items 1-32 are attached hereto as Exhibits 2-33, respectively.

1. Alter, M.J. (1997) "Epidemiology of Hepatitis C" *Hepatology*, 26:625-655 (Exhibit 2);
2. Chien, C., et al. (1991) "The two-hybrid system: a method to identify and clone genes for proteins that interact with a protein of interest" *Proc. Natl. Acad. Sci. U.S.A.*, 88:9578-9582 (Exhibit 3);
3. Choo, Q.-L., et al. (1989) "Isolation of a cDNA clone derived from blood-borne nonA, nonB viral hepatitis genome" *Science*, 244:359-362 (Exhibit 4);
4. Choo, Q.-L., et al. (1991) "Genetic organization and diversity of the hepatitis C virus" *Proc. Natl. Acad. Sci. U.S.A.*, 88:2451-2455 (Exhibit 5);

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5. Chang, R.-Y., et al. (1997) "Requirement of the DEAD-box protein Dedlp for messenger RNA translation" *Science*, 275: 1468-1471., (Exhibit 6);
6. Fields, S., and Song, O. (1989) "A novel genetic system to detect protein-protein interactions" *Nature*, 340:245-246 (Exhibit 7);
7. Fukushi, S., et al. (1997) "The sequence element of the internal ribosome entry site and a 25-kilodalton cellular protein contribute to efficient internal initiation of translation of hepatitis C virus RNA" *J. Virol.*, 71:1662-1666 (Exhibit 8);
8. Gee, S. L., and Conboy, J. G. (1994) "Mouse erythroid cells express multiple putative RNA helicase genes exhibiting high sequence conservation from yeast to mammals" *Gene*, 140: 171-177 (Exhibit 9);
9. Hsieh, T.-Y., et al. (1998) "Hepatitis C virus core protein interacts with heterogeneous nuclear ribonucleoprotein K" *J. Biol. Chem.*, 273, 17651-17659 (Exhibit 10);
10. Kato, N., et al. (1990) "Molecular cloning of the human hepatitis C virus genome from Japanese patients with non-A, non-B hepatitis" *Proc. Natl. Acad. Sci. U.S.A.*, 87:9524-9528 (Exhibit 11);
11. Kim, J. L., et al. (1998) "Hepatitis C virus NS3 RNA helicase domain with a bound oligonucleotide: the crystal structure provides insights into the mode of unwinding" *Structure*, 6:89-100 (Exhibit 12);
12. Kim, D. W., et al. (1994) "Trans-suppression of gene expression by hepatitis C viral core protein" *Jpn. J. Med.*

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Sci. Biol., 47:211- 220 (Exhibit 13);

13. Kuo, G., et al. (1989) "An assay for circulating antibodies to a major etiological virus of human non-A, non-B hepatitis" *Science*, 244:359-363 (Exhibit 14);
14. Lanford, R. E., et al. (1993) "Analysis of hepatitis C virus capsid, E1, and E2/NS1 proteins expressed in insect cells" *Virology*, 197:225-235 (Exhibit 15);
15. Leroy, P., et al. (1989) "The protein encoded by a murine male germ cell-specific transcript is a putative ATP-dependent RNA helicase" *Cell*, 57:549-559 (Exhibit 16);
16. Liang, T. J. (1998) "Combination Therapy for Hepatitis C Infection" *N. Eng. J. Med.*, 339: 1549-1550 (Exhibit 17);
17. Mamiya, N., et al. (1997) "Epidemiology, prevention, clinical features and therapy of hepatitis B, C and G" *Current Opinion in Infectious Diseases.*, 10:390-397 (Exhibit 18);
18. Matsumoto, M., et al. (1996) "Homotypic interactions and multimerization of the hepatitis C virus core protein" *Virology.*, 218:43-51 (Exhibit 19);
19. Matsumoto, M., et al. (1997) "Hepatitis C virus core protein interacts with the cytoplasmic tail of lymphotoxin- β receptor" *J. Virol.* 71:1301-1309 (Exhibit 20);
20. Moradpour, D., Kary, P., Rice, C. M., and Blum, H. E. (1998) "Continuous human cell lines inducibly expressing hepatic C virus structural and nonstructural proteins" *Hepatology*, 28:192-201 (Exhibit 21);

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21. National Institutes of Health Consensus Development Conference Panel Statement (1997) "Management of Hepatitis C" *Hepatology*, 26:2S-10S (Exhibit 22);
22. Okamoto, H., et al. (1991) "Nucleotide sequence of the genomic RNA hepatitis C virus isolated from a human carrier: comparison with reported isolates from conserved and divergent regions" *J. Gen. Virol.*, 72:2697-6704 (Exhibit 23);
23. Ray, R. B., et al. (1996) "Hepatitis C virus core protein cooperates with ras and transforms primary rat embryo fibroblasts to tumorigenic phenotype" *J. Virol.*, 70:4438-4443 (Exhibit 24);
24. Ray, R. B., et al. (1997) "Transcriptional repression of p53 promoter by hepatitis C virus core protein" *J. Biol. Chem.*, 272:10983-10986 (Exhibit 25);
25. Reynolds, J. E., et al. (1995) "Unique features of internal initiation of hepatitis C virus RNA translation" *EMBO J.*, 14:6010-6020 (Exhibit 26);
26. Rozen, F., et al. (1990) "Bidirectional RNA helicase activity of eucaryotic translation initiation factors 4A and 4F" *Mol. Cell Biol.*, 10:1134-1144 (Exhibit 27);
27. Selby, M. J., et al. (1993) "Expression, identification and subcellular localization of the proteins encoded by the hepatitis C viral genome" *J. Gen. Virol.*, 74:1103-1113 (Exhibit 28);
28. Suzuki, R., et al. "Nuclear localization of the truncated hepatitis C virus core protein with its hydrophobic C terminus deleted" *J. Gen. Virol.*, 76:53-61 (Exhibit 29);

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29. Takamizawa, A., et al. (1991) "Structure and organization of the hepatitis C genome isolated from human carriers" *J. Virol.*, 65:1105-1113 (Exhibit 30);
30. Yao, N., et al. (1997) "Structure of the hepatitis C virus RNA helicase domain" *Nat. Struct. Biol.*, 4:463-467 (Exhibit 31);
31. Ye, Q., and Worman, H. J. (1996) "Interaction between an integral protein of the nuclear envelope inner membrane and human chromodomain proteins homologous to *Drosophila* HP1" *J. Biol. Chem.*, 271:14653-14656 (Exhibit 32);
32. Zhu, N., et al. (1998) "Hepatitis C virus core protein binds to cytoplasmic domain of tumor necrosis factor (TNF) receptor 1 and enhances TNF-induced apoptosis" *J. Virol.* 72:3691-3697 (Exhibit 33);

Applicants request that the Examiner review the references and make them of record in the subject application.

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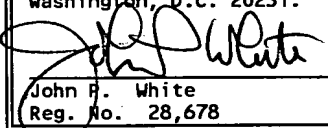
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. If any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
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